



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Attorney Docket No. 00-1282)

In re Application of:

Therese Jourdiar

Serial No.: 09/720,513

Filed : March 26, 2001

For: Mucosal Targeting Immunization

Group Art Unit: 1648

Examiner: Bao Qun Li

Conf. No.: 3546

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW
REMARKS PURSUANT TO OG NOTICE OF 12 JULY 2005

Dear Sir:

Applicant respectfully requests a Pre-Appeal Brief Review in the above application. This paper sets forth Applicant's concise statement of clear errors in the Examiner's rejections.

35 U.S.C. § 103 REJECTIONS

1. Claims 10-15 stand rejected as obvious over Carrano et al., (WO 95/26718), Grosswater et al. (*Pediatrics*, (1997) **100**:400-403), Stites et al., (*Medical Immunology*, (1997) pg.782, Stites, et al. Eds., Appleton & Lange, Stamford, CT), and Bouvet et al. (*Infect. Immun.*, (1994) **62**:3957-3961) and "as substantiated by Anderson et al. (*J. Infec. Dis.*, (1989) **160**(6):960-969) and Nell Tharpe (Google Books.)." Office Action, dated December 13, 2005, page 2.

SUMMARY OF APPLICANT'S ARGUMENT

The invention is directed to a method of inducing in a human a systemic immune response and a local immune response of antibodies (IgA, IgG, or IgM) or B cells secreting those antibodies that is targeted at the rectogenitourinary mucous membrane and the lymph nodes which drain it, comprising parental administration, to the thigh, of a composition comprising an effective amount of an immunogen of an agent having a gateway into the rectal, genital and/or urinary mucous membranes. (See, e.g., Pending Claim 10).

Applicant respectfully submits that the pending rejections are improper because they fail to establish a *prima facie* case of obviousness for the following reasons:

- A. The rejections are legally insufficient because they allege only a generalized suggestion to make the claimed invention and not a particularized suggestion.
 - B. There is no suggestion or motivation to combine the elements of the cited art as has been done in the pending rejections.
 - C. Even were one to combine the references as proposed, the combination would not result in all the elements of the pending claims.
 - D. The cited art does not provide teachings that would imbue the ordinary artisan with a reasonable expectation of success.
 - E. The results achieved are unexpected.
- A. The rejections fail to identify a particularized suggestion/motivation to make the particular claimed invention.

The law requires something more than a general motivation or suggestion to support an obviousness-type rejection; it requires that the suggestion or motivation be particularized, i.e., directed to the invention being claimed, with all the claim limitations. *In re Deuel*, 34 U.S.P.Q.2d 1210, 1215 (Fed. Cir. 1995) (the prior art must suggest the particular form of the invention and how to make it; general guidance is insufficient); *In re Obukowicz*, 27 U.S.P.Q.2d, 1063, 1065 (Bd. Pat. App. Int. 1992) (Prior art “that gives only general guidance and is not at all specific as to the particular form of the claimed invention and how to achieve it . . . does not make the invention obvious.”).

The Office has stated that “the cited references...provide a strong motivation for the person with ordinary skill in the art to use the claimed method of thigh injection for inducing [] high levels of long-lasting antibodies, which might be protective against the corresponding pathogen in the genital area as suggested.” See, e.g., Office Action dated 07/29/03, ¶ 6. However, this is simply a generalized motivation/suggestion that would be applicable to any method of immunizing a human to generate “high levels of long-lasting antibodies.” At the most, it is merely a desire to induce a strong immune response. The references do not provide particular motivation for a) generating both a local and systemic immune response by b) administering to the thigh a composition comprising an immunogen of a pathogenic agent having a gateway into the rectal, genital and/or urinary mucous membranes). As such, this motivation/suggestion is insufficient as a matter of law.

B. There is no suggestion or motivation to combine the particular asserted elements of the cited art to arrive at the presently claimed invention

Carrano *et al.* is relied upon for its teaching of a method of immunizing an individual against, *e.g.*, HIV, HPV, Herpes simplex 1 & 2, etc., by intramuscular administration of a genetic construct (*i.e.*, DNA- or RNA-based compositions) to the individual. See, *e.g.*, the Office Actions dated 02/13/03, 7¶ and 04/05/04, 6¶. Carrano fails to teach a) any particular muscle for administration, and b) generation of both a systemic and a local immune response. Further, Carrano *et al.* teaches that the compositions require a “genetic vaccine facilitator” such as anionic lipids, saponins, lectins, estrogenic compounds, hydroxylated lower alkyls, DMSO, and urea.

Groswasser *et al.* and Stites *et al.* are relied upon for their teaching of intramuscular injection to the thigh.

Bouvet *et al.* is relied upon for its teaching that parenteral injection of the tetanus toxoid vaccine leads to systemic immune response, including the presence of systemic-derived IgG antitoxins in vaginal secretions. Bouvet *et al.* suggests that parenteral vaccination could be used against sexually transmitted pathogens, as a substitute for local immunization, when local immunization is unavailable, or to complement local immunization. (See p. 3959.) However, Bouvet *et al.* were unable to generate a local immune response (as evidenced by secretory IgA production) via a parenteral injection. (*Id.*) Further, Bouvet does not teach or suggest parenteral administration to the thigh.

What the pending rejections fail to do is to identify suggestions in the references themselves or from knowledge commonly available to those skilled in the art as to why one of ordinary skill in the art would select these particular elements for combination from among all the particular teachings of these references and, indeed, from all the prior art. While each reference may teach a particular element of the present claims, each fails to provide any suggestion or motivation to combine the elements as has been done in the pending rejections. It is not sufficient that the prior art teach administration to the thigh or vaccination with an immunogen of a pathogenic agent having a gateway into the rectal, genital and/or urinary mucous membranes, for example. What the prior art must suggest or motivate is the **combination**, *i.e.*, administration to the thigh of a composition comprising an immunogen of a pathogenic agent having a gateway into the rectal, genital and/or urinary mucous membranes to yield a systemic immune response **and** a local immune response that is targeted to the rectogenitourinary mucous membrane and the lymph nodes which drain it. The rejections have failed to do this.

C. Even were one to combine the references one would not arrive at the presently claimed invention

The combination of the cited art does not result in the presently claimed invention. None of the cited art teaches even a general induction of both a local and a systemic immune response, let alone a systemic and a local immune response targeted at the rectogenitourinary mucous membrane and the lymph nodes which drain it, wherein the response is directed against pathogens having a gateway into the rectal, genital and/or urinary mucous membranes, as recited in the claims.

D. The cited art does not provide teachings that would imbue the ordinary artisan with a reasonable expectation of success.

The Applicants respectfully submit that the Examiner has also failed to establish a *prima facie* case of obviousness because the teachings of the cited references do not provide a sufficient basis for the ordinary artisan to derive a reasonable expectation of success of achieving the claimed invention. Bouvet *et al.* teach that “[s]ystemic-derived immunity in human genital secretions reinforces the potential interest in vaccines given by the parenteral route in prevention of sexually transmitted diseases.” (Page 3960). However, this reference teaches that parenteral vaccinations can induce only a systemic-derived antibody response; the parenteral injection was ineffective at producing a local immune response. The authors are explicit on this point: “A significant involvement of the local immune system at the early phase of boosting (day 10), as well as at the late phase of the previous vaccination (day 0), seems to be unlikely, since the level of SIg antitoxins was low enough in genital secretions to be explained solely by the active transport of serum-derived polymers across epithelial cells ...” (page 3960, right column). Thus, nothing in this reference provides a basis for a reasonable expectation of success of achieving both a systemic and a local immune response targeting the rectogenitourinary mucous membrane and the lymph nodes which drain it. The disclosures of Stites *et al.*, Groswasser *et al.*, and Carrano *et al.* (discussed in Section B, above) fail to provide any additional support for a reasonable expectation of success, and therefore, they do not provide a person having ordinary skill in the art with a reasonable expectation of success in achieving the entire scope of the invention as defined by the pending claims.

E. The results achieved are unexpected

During prosecution, Applicants submitted three Rule 1.132 Declarations executed by Dr. Therese-Marie Jourdier. The Declarations provide data and Dr. Jourdier’s conclusions from experiments related to administration of an HIV antigen (“gp160”) to monkeys in various locations and measuring the resulting immune response. Dr. Jourdier attested that:

- Administration of the antigen to the thigh produced about 18-350 times the specific antibody response in the iliac and inguinal lymph nodes compared to submaxillary and axillary lymph nodes and in blood. Also, specific antibody was detected in rectal and vaginal ("V/R") washes as well as in urine. This showed that the induced immune response was targeted to the rectogenitourinary lymph node system and its mucous membranes. (Declaration executed on 10/21/2003, ¶¶7-9).
- Antigen administered directly to the target site (V/R) failed to induce specific antibody in V/R secretions, while thigh administration induced specific antibody in V/R secretions. When combined, administration of antigen to the thigh and direct administration of antigen to V/R did not boost the initial immune response induced by thigh administration alone. One skilled in the art could not have expected that antigen administered to the thigh would result in a specific response in a distal site, *i.e.*, the rectogenitourinary lymph node system and mucous membranes. Nor would one have expected that a specific immune response could have been induced in the rectogenitourinary region by distal (*i.e.*, thigh) administration whereas a specific immune response would not be elicited even when antigen was administered directly to the target site (*i.e.*, V/R). (Declaration executed on 02/28/2005, ¶¶8-10).
- Administration of antigen to the thigh induced a substantially and significantly greater specific antibody response in the rectogenitourinary region when compared to the response induced by administration to the deltoid, evidencing that not all intramuscular injections yield the same results. (Declaration executed on 09/19/2005, ¶8).


Conclusion

For all the reasons presented above, the Office has failed to present a proper basis for an obviousness rejection under 35 U.S.C. § 103. Accordingly, Applicants respectfully request that the obviousness rejections be withdrawn.

Respectfully submitted,

Dated: March 13, 2006

By:


Michael S. Greenfield, Ph.D.
Reg. No. 37,142